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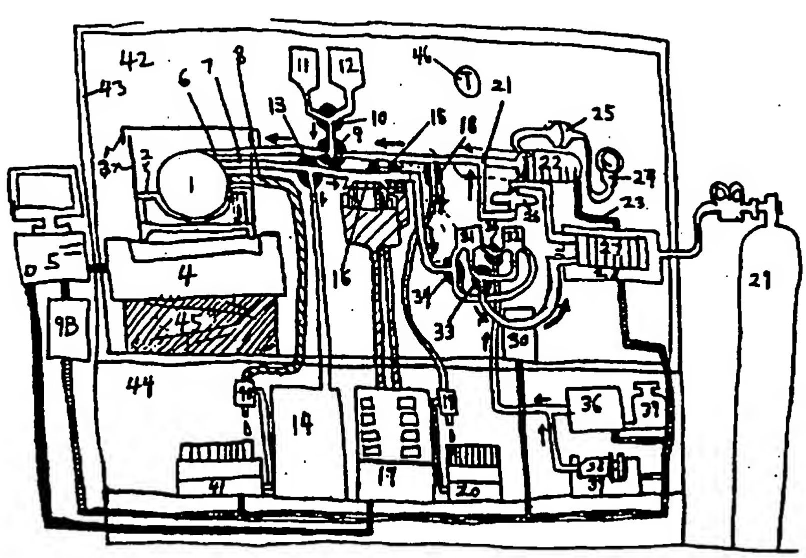


(57) Abstract

A computer-based organ perfusion apparatus is described which is capable of perfusing organs (1) at near-normal temperatures with blood or other oxygen-carrying substances. The apparatus permits organ viability to be evaluated by on-line measurements of physiological performance. Embodiments of the apparatus use a computer-driven blood pump (30) to allow physiological perfusion conditions to be established. The apparatus includes provisions (48) for the replacement of lost circulating volume and for the infusion of nutrients, drugs, and altered perfusates to assist in maintenance or recovery of organs. The apparatus may further sense perfusate gas tensions, pH, and temperature without electrical cross-interference (15 and 16), automatically measure production rates of urine, bile, pancreatic duct secretions, or other physiological exudations (8), and determine organ blood or perfusate flow rates, vascular resistance, and organ edema (4).

ORGAN EVALUATION AND RESUSCITATION DEVICE AND METHOD

BACKGROUND OF THE INVENTION

The invention relates to a method and apparatus for perfusing an organ. The perfusion of the organ permits the viability of the organ to be maintained and evaluated. Further, the perfusion of the organ by certain perfusates or fluids, including blood, can resuscitate the organ to a point where it is viable.

The shortage of donor organs for transplantation has been a long-term problem which has seen very little improvement over the past 10 years. There are very few donors with organs that are viable and able to be effectively transplanted. It has been estimated that the number of potential donors would double if it were possible to use organs after the cardiac arrest of potential donors. This could increase the net number of available organs from the current 5,000 donors or so to about 10,000 donors per year in the U.S., with the addition of perhaps another 5,000 donors per year outside of the U.S.

Certain organs are known to be viable after as long as 30 to 60 minutes or more of warm ischemia, based on animal studies. In these studies, the flow of fluid to individual organs was selectively interrupted and then re-established. However, when flow to the organ is interrupted by irreversible cardiac arrest or blood loss of a potential organ donor, organ resuscitation is more problematic. A machine into which an organ can be placed to permit the organ to be reperfused under controlled conditions is needed. A machine of this type would terminate the ischemic insult and allow the organ to begin to self-repair.

The device would also be useful if a potential donor has suffered cardiac arrest. The device can be used between cardiac arrest and organ excision for perfusion in

perfusate volume. None has described a disposable circuit, provisions for maintaining perfusion for lengthy periods by permitting replacement of lost fluid volume and of metabolized nutrients, or provisions for changing perfusate composition either gradually or abruptly, all of which are features that may be required for optimal organ resuscitation. In addition, the Sadri and the Martindale devices are directed toward perfusion of hearts, and Rijkmans' work emphasizes the importance of normothermic perfusion of kidneys, whereas equipment is needed that can be used to perfuse any organ.

Pacini et al., 56 Boll. Soc. Ital. Biol. Spec., 2497-2503 (1980) and 6 Renal Physiol., 72-79 (1983) showed that rabbit kidneys could be maintained in a good functioning state for over an hour during normothermic blood perfusion. This perfusion required the removal of leukocytes and platelets from the blood prior to use. Perfusion under such conditions might allow damaged organs to recover prior to subsequent cooling and storage or transplantation. Similarly, oxygen-carrying compounds other than blood may maintain and restore function near normothermia. However, Pacini did not describe useful apparatus for resuscitating organs nor the use of a computer.

Another desirable feature for the organ transplantation field is a means which can assess the viability of an organ prior to transplantation. Recently, claims have been made that organ vascular resistance provides an adequate test of organ viability. These claims must be evaluated in the light of a vast amount of literature which states the contrary.

Fahy et al., 31 Cryobiology, 573 (1994) reported that the viability of rabbit kidneys after former cryoprotectant perfusion was predicted by blood reflow rates manually measured in the first 45 minutes of blood reflow. However, quantifying vascular resistance by manual means is not practical for routine organ processing. Khirabadi and Fahy, 31 Cryobiology, 10-25

perfusate. Previously described apparatus has not considered the significance of ambient humidity. Further, there has been no consideration of organ surface drying. Finally, previous apparatus has not provided a sheltered environment to minimize the chance of bacterial contamination.

There is considerable literature on the perfusion cooling of heart-beating cadavers for multiorgan procurement. It has been found that such perfusion can adequately preserve internal organs without conflict. Application of this technique after cardiac arrest, rather than before cardiac arrest, could help to salvage organs that are now abandoned. It is urgent, therefore, that similar techniques be available to be used after cessation of cardiac function. Thus, organs that are currently lost can be salvaged. Standard heart-lung machines are capable of initiating in vivo perfusion and reoxygenation after cardiac arrest, however they cannot follow through on reversing damage. Further, heart-lung machines cannot document the in vivo perfusion conditions or connect this information with the conditions used for, and the results of, subsequent regeneration of each procured individual organ in vitro.

SUMMARY OF THE INVENTION

The instant invention provides a perfusion apparatus and method for perfusing organs which overcome the above noted deficiencies of conventional perfusion apparatuses and methods. Specifically, the invention provides a perfusion apparatus and method with an automatically controlled and monitored fluid system. The system includes a controller and monitors for the organ and the fluid. In preferred embodiments, the controller measures the viability of an organ, as well as measuring and controlling various characteristics of the perfusion fluid. The perfusion system may be made of blood-compatible materials, although fluids other than blood can be used. Useful perfusates include fluids selected from the group comprising blood, modified blood, ordinary

that is suitable for use on human or animal organs that may be later transplanted. Fluid systems having different volumes may be provided for different sized organs. The modular fluid system permits a sterile and economical construction from known components.

Preferred embodiments include an organ transfer platform, preferably a position-adjustable platform. The platform eliminates the need for direct handling of the organ. The platform prevents the organ from changing orientation after removal from the donor and before placement in the perfusion apparatus. The platform presents the organ in a flexible manner which facilitates connection of the organ to the apparatus. The platform can also prohibit unwanted and potentially hazardous vascular motions. Artery and vein positions can be adjusted according to the natural requirements of each organ. These positions are then firmly held in position avoiding any danger to the organ during attachment to the perfusion system.

Fluid can be moved through the system by a pump which is non-traumatic to blood or other synthetic or natural perfusion fluids such as emulsions. A computer controlled adjustable piston-cylinder blood pump is preferred. However, other types of pumps can be used if desired. The pump controls the pressure of the infused fluid in the fluid system.

Furthermore, the apparatus can control independently the infusion of nutrients, drugs and alternate perfusates into the fluid in the fluid system, thus permitting the organ to receive vital and beneficial material. For example, the controller can actuate valves and/or pumps connected to liquid sources. This is especially beneficial if the organ is damaged so that the addition of the nutrients or pharmaceutical agents can resuscitate the organ.

The use of a blood pump also allows for a pulsating perfusion to simulate the natural in vivo environment of the organ. The pressure pulse wave can be

on the organ) can be replenished at the same rate volume is lost. Uncompensated loss of volume will result in altered hematocrit, plasma protein concentration, perfluorochemical emulsion concentration, etc. The continuous replacement can be accomplished by sensing the lost volume directly or indirectly, and activating an appropriate pump or pumps to supply additional solution to the perfusion system. This permits avoidance of the recycling of excreted fluids which may damage the organ.

The device is also capable of continuously replacing substrates in the perfusate or fluid at the rate they are consumed by the perfused organ. The replacement can be based on standard rates of substrate utilization or on rates of substrate utilization previously measured in similar organs. Substrate replacement and volume replacement can be accomplished independently of each other.

The computer controlled system can be adjusted to permit either a gradual or abrupt change in the perfusate. One example of a gradual change would be gradual replacement of a low-viscosity crystalloid perfusate with leukocyte and platelet depleted blood. An abrupt change could include a switch from blood to saline and/or a switch from saline to fixative for experimental runs, with collection of fixative or other perfusate in an auxiliary reservoir.

The perfusion apparatus can challenge organs by infusing pharmaceutical, physiological or rescue agents under the control of the controller. The controller can control the onset time, administration rate, rest periods, etc. of this infusion.

Further, the perfusion apparatus can be used to perfuse a cadaver donor. The perfusion apparatus can then accommodate one or more organs from the donor as organ procurement proceeds and is completed.

The perfusion apparatus or portions thereof, especially including the connection to an organ, may be enclosed in a sterile or semi-sterile climate-controlled

interface board (the PBM-4 Minarik Process Control Module, Shingle Gibbs, Inc. Baltimore, Md) ran the Harvard Apparatus Blood Pump and was directly mounted inside the blood pump housing. A custom electrical system was supplied by Eldex Inc. to allow drop detection by the computer.

The Perfusion System

Fig. 1 presents a schematic diagram of the perfusion system. The fluid-conducting elements of the system may be prefabricated as one disposable pack that can be introduced into the equipment as a unit. The system may also be composed in whole or in part of modules that can be connected by using sterile Luer Lok™ fittings and piercing fittings, such as blood bag and blood bag tube spikes. For example, blood bag tubing spikes may be used to insert lines into mating inlet and outlet ports of pump 30. Optionally, a male or female Luer fitting may be used to effect this connection.

When the perfusate is blood or modified blood, the tubing used is preferably blood-compatible tubing such as blood bag tubing, Tygon® tubing, or Silastic® tubing.

The organ 1 is atraumatically supported on a special organ holder and transport platform 2. Platform 2 organizes the renal vessels after organ excision and prior to perfusion in vitro. The organ transport platform 2 is placed into an organ container 3. Container 3 provides general protection for the organ and may, when the organ is electrically excitable, such as a heart, be used to facilitate mounting of electrodes used to monitor and/or pace electrical activity. It also prevents platform 2 from contacting the top loading balance 4. This further ensures the sterility of organ 1.

The organ container 3 and the organ platform 2 are designed to allow free access to the organ 1. Openings in the container wall allow cannulae to enter and exit. Platform 2 and container 3 may be combined into a single unit if desired. The outer container 3 could be eliminated or replaced by a piece of stretched parafilm.®

secretion/excretion line 8. Fluid or perfusate is delivered to the organ 1 from the arterial line 6 and drained from the organ 1 by the venous line 7. The vein is cannulated in order to permit measurements of oxygen consumption, carbon dioxide production, and blood acidification as indices of the fundamental metabolic balance sheet of the organ 1. Correction for losses of oxygen and carbon dioxide in any secretions or excretions is not significant because the volume of secretions from organs, including urine flow in kidneys, is normally such a small fraction of total organ blood flow and because the oxygen and CO_2 carrying capacity of these secretions is low in comparison to blood. Oxygen consumption, CO_2 production, and acid production are calculated from measurements of gas tensions and pH in the arterial line 6 at sensor bay 15 and in the venous line 7 at sensor bay 16 using standard formulas.

Sensor bays 15 and 16 are CDI sensor heads (made by 3M Health Care, Tustin, California) or an equivalent. CDI heads also measure arterial and venous temperatures, to check on temperature control and uniformity within the perfusion cabinet 42. The CDI heads are connected to a readout device 17. Readout device 17 sends a signal to the computer 5 via a serial port. CDI sensors or equivalents are selected because they are able to collect the data without electrical interference.

In Figure 1 reservoirs or containers 11 and 12 may be provided to hold fluid. The fluid is significantly different in composition from the blood or other solution travelling through the system. A waste collection reservoir 14 may be provided to drain undesired perfusate.

Manual or computer-actuated valves 9, 10, 13, 18, 33, 34, 35, and 45 are provided in the fluid system. Elements 18 and 45 are pinch-type solenoid valves (such as the Model 100P2WNC valves sold by Bio-Chem Valve Co., East Hanover, NJ) capable of blocking lines 48 and 49.

Valve elements 9, 10, 13, and 33-35 are preferably three-way (rather than two-way) valves. These valves may

13 are activated immediately thereafter so as to permit fluid from reservoir 11 to drain into arterial line 6, proceed through the organ 1, and exhaust to drain site 14 through valve 13. Typically, reservoir 11 will contain saline to flush blood from the organ 1 that would otherwise become trapped in the organ by the fixative in 12. After the saline rinse from reservoir 11, valve 10 is activated to allow the contents of reservoir 12 (typically fixative) to flow through the organ instead of the contents of reservoir 11.

Fluid from reservoirs 11 and 12 may drain into the organ 1 under the influence of gravity. Alternatively, the fluid may be propelled by a pump (not shown) placed between 9 and 10.

Reservoirs 11 and 12 are preferably within the temperature-controlled cabinet. Therefore, fixation can proceed without changing organ temperature.

The positioning of valves 9 and 13 between the organ and sensor bays 15 and 16 results in the organ being fixed without contamination of the sensor heads, perfusion pump, pressure transducer, or other vulnerable and reusable system components with fixative.

Upstream of arterial sensor bay 15 is an entry site for arterial infusion line 48. Line 48 permits the delivery of rescue drugs from syringe 46 under the control of computer-actuated syringe pump 47. The use of a syringe and a syringe pump is not critical, another type of equivalent reservoir and fluid metering system being acceptable. The infusion entry site is guarded by pinch valve 45 preventing the contamination of line 48 by perfusate and preventing unwanted contamination of the active perfusion circuit with drug.

Upstream of line 48 is the exit point for arterial blood sampling. This point is governed by pinch valve 18 and leads to the fraction collector 20 and the associated drop counter 19. Drop counter 19 is used to ensure collection of a consistent volume with each blood collection (typically about 2 ml). As noted above, line

valves could be added to enable additional complexity using the same approach.

Valve 35 is complementary to valve 33. When the perfusate of bag 31 has switched to the perfusate of bag 32, any volume replacement or nutrient replacement should also be transferred from bag 31 to bag 32 using valve 35. Of course, the fluid delivered for volume replacement from the reservoir 37 by the pump 36, and the vehicle for the nutrients in syringe 38, as delivered by computer-actuated syringe pump 39, must also be compatible with the perfusate composition of the bag 32. If it is not compatible, a similar three-way valve or a flow-through 3-way valve, would be need to be interposed between 36 and 37 to permit a different volume replacement solution to be chosen instead of the solution in reservoir 37 to ensure compatibility with the new perfusate. Fortunately, the volume of infused nutrient solutions is expected to be small enough, and the vehicle solution is expected to be universal enough, to preclude the need for separate nutrient solution infusions for separate perfusates most of the time.

Valve 34 is similar to valve 35 in that it controls which bag, 31 or 32, receives incoming fluid. In valve 34, the incoming fluid is venous return from the perfused organ. Note that bags 31 and 32 are located vertically below or at the level of the organ 1, not substantially above it. This is to avoid creation of a substantial venous outflow pressure that would slow perfusion and promote organ edema.

It would be desirable to measure venous pressure to ensure that it remains within the desired limits. This measuring capability can be incorporated in a manner similar to the inclusion of the arterial pressure transducers 22 and 24.

The secretion collection line 8 leads to drop counter 40 in route to fraction collector 41. The drop counter 40 is a standard unit used with laboratory fraction collectors. Its output is directed to the

The cannula control area 218 consists of a main body 201 and a retainer bar 204. The retainer bar 204 mates with the main body 201 by means of the hinge 205 and the thumbscrew 206. Bar 204 may be pivoted up to allow organ cannulae to be laid on the floor 219 of the main body 201 without restriction of any kind on the lateral position or rotational orientation of these cannulae. The bar 204 may then be lowered and locked in place with thumbscrew 206 or other suitable means to immobilize the cannulae and/or their associated tubing in the previously-selected, preferred positions. The immobilization is attained by placing vertical downward pressure on the cannulae and/or tubing according to the relative heights of the cannulae or tubing cross-section and the gap 207, which is determined by the construction of the recess 219 receiving the bar 204. The recess 219 is in the lateral wall of base portion 201. The height of the gap 207 is selected to meet the requirements of the specific cannulae and/or tubing used. It should be chosen to apply sufficient pressure to immobilize the tubing and/or cannulae without collapsing the tubing/cannulae significantly. The vertical elevation of the recess floor 222 and the bar 204 are selected to suit the type and size of the organ being perfused.

Often the vertical height of the vessels emerging from an organ 213 is not what is expected. In this case, since the floor 219 of base 201 is horizontal and at a fixed elevation, an angle can be imposed between the horizontal tip of the cannula near the organ and the organ vessel leading from the organ to the cannula tip. This angle may alter the flow through the organ and damage the organ vessel. To avoid this problem, the base 201 is constructed to pivot within the organ cradle part 217. Thus a straight line path from the cannula tip to the organ can be achieved by altering the horizontal disposition of the cannula. This is attained by incorporating pin 203 and lever 202 in the cannula control base 201 and by incorporating thumbscrew 210 and holes 209

or later organs can be added to the machine as they are procured. The lines 6 and 7 of Fig. 2 can be excluded from the system when all organs have been collected. In Fig. 3, the reservoirs, pump, oxygenator, and tubing are enlarged to be appropriate for use on a cadaver.

Valve Construction

The construction of the three-way externally occluding valves 9, 10, 13, and 33-35 is described with respect to Figs. 4 and 5.

The tubing to be occluded is configured in a "T" pattern. In Fig. 4, tubing segment 402 leads to the organ while tubing segment 403 leads from the main perfusate source, and tubing segment 401 leads from the bags 11 and 12 as seen in Fig. 1. Thus, the primary or normal flow is from 403 to 402, with 401 being blocked. The secondary flow direction is from 401 to 402, with 403 being blocked.

In Fig. 4A, four arc-shaped fingers 404-407 are similarly shaped and shown end-on. The fingers 404-407 project past the segments of the tubing. Each finger 404-407 is attached to a rod 408-411. Each rod 408-411 can be rotated about its axis by a suitable means (not shown). In the normal flow pattern, rod 408 is rotated clockwise and rod 409 is rotated counter-clockwise. This movement forces fingers 404 and 405 toward each other, thereby occluding tubing segment 401. Tubing segments 402 and 403 remain unaffected. To switch to the secondary flow pattern, the rod 409 is rotated clockwise and rod 411 is rotated counter-clockwise. This brings fingers 405 and 407 together, thereby occluding tubing segment 403. Rod 404 is also rotated counter-clockwise back to its "rest" position, shown in Fig. 4A. This removes deformation of tubing segment 401 without affecting tubing segment 402.

Finger 406 is not used during a perfusion, but may by used during preparation of the circuit prior to perfusion. With fingers 405 and 407 in their rest positions, rotating finger 404 counter-clockwise and finger 406 clockwise occludes the tubing segment 402, while segments 401 and 403 remain open. This

RESULTS

Fig. 6 presents the perfusion data for a recent experiment using a rabbit kidney. The data are shown in the format displayed on our monitor in real time. All graphs have the same time base and are displayed as a series of parallel strips. The organ used in the tests was a rabbit kidney. The kidney was perfused with leukocyte and platelet depleted rabbit blood with some hemodilution with a saline/nutrient solution containing hydroxyethyl starch to combat edema.

Trace 1 shows organ weight demonstrating minimal edema formation with perfusion time.

Trace 2 shows that pressure was excellently controlled by the computer. The computer registered systolic (upper thin line), mean (middle heavy line) and diastolic (lower thin line) pressure continuously. The pressure was initially elevated to the target 90 mmHg level gradually to avoid pressure overshoot. Pressure was maintained constant in Trace 2 despite continually improving blood flow, as evidenced by Trace 3. The continually improving blood flow is evidence of organ damage reversal and increased organ viability.

Urine flow rate is shown in Trace 4. The urine flow rate shows continuous improvement after about 40 minutes.

Trace 5 shows the temperature being maintained at the 35-36 degree Fahrenheit target range. This range was chosen because slight hypothermia is known to favor repair in vivo and is advantageous. Any temperature from about 20 degrees to about 37 degrees Fahrenheit may permit organ function to be determined and improved.

The kidney rapidly consumed oxygen which was dissolved in the solution, as shown in Trace 6. This is also evidenced in the calculated oxygen consumption for the kidney as shown in Trace 9. Trace 9 shows more oxygen consumption between time zero and 60 minutes, than after that time. This suggests that some oxygen consumption is being used for organ repair during the first 60 minutes.

A physiological environment is recreated in the blood apparatus. Blood is pumped by suitable pump, for example by a Harvard pulsatile blood pump, through a closed system of blood compatible tubing. The blood is stored in a 250 ml blood collection bag, for example, by Fenwal on a venous line. The blood circulates at constant pressure through the kidney, whose artery, vein and ureter have been canulated. Pressure is detected through a pressure transducer, for example, PX23 by Ohmeda, which signals a computer that in turns sets a pumping rate for the blood pump.

The blood is oxygenated by passing through a coil of siliconic tubing in an oxygen saturated chamber. The gas composition of the blood is continually recorded by a blood gas analyzer, such as a CDI blood gas analyzer. The system is equipped with a 40 micron microaggregate filter, for example, by Baxter on the arterial line.

The volume of urine produced is measured by a drop counter data, for example, by Eldex, and an equivalent volume of fluid is returned to the blood bag. Thus, the perfusate composition is kept constant. A modified Weinberg solution reservoir is connected to a 0.22 micron filter, for exmaple, by Millipore, through a return line to the blood bag. A roller pump, for example, by Masterflex, is programmed so the pump rate is monitored according to the volume of urine produced. When added to the blood, the Weinberg solution allows to keep the electrolytes and hemotocrit at a constant level.

The system described above, is positioned on top a water bath, and is covered. This maintains the required normothermic temperature and humidity.

Perfusion Fluids

<u>Blood</u>: At least 100ml of blood was drawn from the ear median capillary of three different rabbits in a mixture of asprinc/heparinc (10mg and 1000 mg units). Platelets and white cells were removed by centrifugation to minimize their interference with the perfusion. The hemotocrit is reduced to 25%-30% by adding modified Weinberg solution.

transplantation is done on the left hand side of the rabbit after nephectomy on the left side kidney.

Perfusion

The kidney is perfused with 25-30% hematocrit blood oxygenated at a pressure of at least 120 mmHg. The perfusion pressure is maintained and controlled at 90 mmHg for 2 hours. Urine is collected by a fraction collector, and the volume measured. Fluid is returned to the blood in an amount equal to the measured volume. Blood samples are collected during the perfusion at time interval of 0, 15, 45, 75, 105 and 120 min. to determine the blood chemistry.

A computer file is generated after the perfusion and data can be graphed as in Fig. 7.

Parameters evaluated

This system allows parameters to be followed, such as blood flow, arterial pressure, urine flow, oxygen consumption. It also allows observation of cortical changes. Oxygen consumption was also evaluated. At precise time intervals, blood and urine samples are collected and their chemistry is an indicator of renal function, such as glomerular filtration, protein exclusion and tubular reabsorption of various chemical substances.

After transplant the rabbits are carefully monitored and their blood creatinine, urea, and other electrolytes. Histology was also performed at the time the rabbit is sacrificed. Glomerula and proximal and distal tubules appearance is observed. The results are summarized in Tables 3 and Figs. 8-16.

A futher embodiment of an organ platform A, as shown in Fig. 17, is provided for the kidney. The organ lies on a soft mesh 2000 that covers an aperture 2001 in a platform 2002. The mesh 2000 is bonded to the platform 2002. A renal artery cannula tubing 2100 and cannula (not shown) generally snaps into a recess 2003 in a positioning bar 2004. This assures a favorable orientation of the artery with respect to the kidney. A further recess 2005 includes two cylindrical pathways through positioning bar

Table 1 = Small Parts List for Composing the Invention

Items	Chemical Nature	Initial item	Characteristics	Model #	Vendor
		when modification have been added			
TUBING	CONNECTION				
Luer Male	Polycarbonate		connectors 3/16'	RMB03041	Gish Biomedical
Luer Female	Polycarbonate		connect to tubing 3/16'	RMA07195	Gish Biomedical
Taper Luer Coupler	Polycarbonate	fit MLLR-9	for male/male connection	MTLC-9	Value Plastics
Taper Luer Square Ring	Polycarbonate	fit MTLC-9	for male/male connection	MLLR-9	Value Plastics
Male Taper to Barb for 1/8"	Polycarbonate	fit RMLLR-9	connector for male rolling luer lock	MTLR230-9	Value Plastics
Male Luer Round ring	Polycarbonate	fit FTLT-9	for manifold / tubing connection	RMLLR-9	Value Plastics
Female Taper T - Luer	Polycarbonate	fit RMLLR-9		FTLT-9	Value Plastics
Silicon tubing: to join some connectors	Silicon Medical Grade		1/8' ID - 1/4' OD 3/16'	T 5715-121	Scientific Products
Blood Bag Tubing	PVC	Taken from Transfer set	Tubing used for blood circulation	4C2243	Fenwal, Baxter
Teflon Connector for the filter	Teflon	Taken from pack	Fit 4C7730	RCM 71M	Stericon
Y- Luer adaptor	PolyUrethane		for pressure & fluid connection	MCY 300	Medcomp
Cannula	Teflon	Silicon tip	1.7 mm ID	500	Neostar
Teflon sleeve	Teflon	from Stericon set	to connect filter	RCM 71 M	Stericon
Transfer set	PVC	with 2 spikes	to connect pump filter/oxygenator	4C2243	Baxter
Filter	PVC	40 um transfusion	after oxygenator	4C7730	Baxter
Filter	PVC	.22 um	for fluid sterility	Millex-GS	Millipore
Filter	PVC		Leucofilter	RC-50	Pall
Bag 150 ml	PVC		for blood Collection	4R2001	Baxter
Bag 300 ml	PL1240		As Nutrient Bag		Baxter
Tube 12 ml	Polypropylene	100 x 13 mm case of 500	Urine Collection	55.516	Sarstedt

Part	Material	Description			
Fraction collector, drop counter, and excitation/readout circuit for data transfer to computer	Polycarbonate		100 x 13	UFC	Eldex
Collection tube				55 516	Starsted
COMPUTER					
Monitor				VGA	
Computer				XT	IBM
Interface				MINI 16	Industrial Computer Source, Inc.
				AO86-P	Industrial Computer Source, Inc.
Software				Misc. Housings	Proprietary
THERMOCOUPLE	Copper/constant	For cage Temperature			Shop made
BALANCE				Galaxy 4000	Ohaus
Nutrient/drug infusion pumps (syringe pumps)				355	Sage Instrument
Volume replacement pump (roller pump)	Masterflex			7016.20	Cole Parmer

Table 4

Summary of the renal function of the perfused kidneys and lists the GFR, Protein exclusion, Na, K, Cl ıd glucose reabsorption

	Min.	GFR Glomerular Filtration Rate ml/min	FF Filtration Fraction (%)	VFR Volume fraction reabsorb (%)	Tubular Reabsorption [Na] (%)	[K] (%)	[Cl] (%)	[Prot] (%)	[Glu] (%)
abbit 2	15	0.810667	4.548397	60.52532	61.34301	23.54571	54.69108	98.90351	56.15976
	45	1.587636	5.077639	70.27027	69.0485	17.0045	61.24517	99.19649	91.32883
	75	4.528333	11.49747	67.27273	68.77005	9.002217	60.19656	99.20177	82.33035
	85	4.55	12.13333	71.42847	74.74654	-27.9503	67.66917	99.20635	50.63492
abbit 7	15	3.110909	5.795062	62.06897	65.35632	24.86737	61.72414	100	90.27409
	45	4.364286	6.6357	70.21277	72.69504	50.66489	67.7305	100	95.31915
	75	3.287143	5.052016	46.15385	51.53846	37.99534	45.17483	100	79.38903
	105	3.091667	4.233951	48.57143	53.87013	33.87755	48.09524	100	66.76923
	120	2.871111	4.192358	52.63158	56.99064	35.08772	52.18471	100	71.57895
	130	3.12	4.541333	50	52.76074	35.71429	48.13084	100	69.56522
abbit 5	15	1.2896	4.232909	75.96154	76.732	17.14403	73.90697	99.27154	88.25393
	45	1.805	5.652775	78.94737	82.70198	0.478469	80.39927	99.36204	97.66082
	75	2.01	5.28441	66.66667	77.22567	11.11111	72.93447	100	99.96377
	105	2.258824	5.269395	57.5	62.68293	28.70968	56.03448	100	99.96205
	120	1.580526	3.834754	51.28205	53.90757	18.80342	45.82228	100	99.60392
abbit 4	15	2.132	6.055433	75	73.51974	32.44681	69.02655	99.21875	98.68421
	45	2.7755	6.5026	67.21311	70.38604	41.62335	65.47222	100	99.6992
	75	3.644176	6.098829	58.53659	62.88768	34.34959	56.71801	100	99.43587
	105	2.453333	3.615148	62.5	35.34483	35.34483	59.77273	99.16667	95.65972
lean	15	1.835794	5.15795	68.3892	69.23777	24.50098	64.83718	99.34846	83.343
	45	2.633106	5.967179	71.66088	73.70789	27.4428	68.71179	99.63963	96.002
	75	3.367413	6.983181	59.65746	65.10547	23.11456	58.75597	99.80044	90.27975
	100	3.088456	6.312957	60	64.23115	17.49544	57.89291	99.59325	78.25648
	120	2.225819	4.013556	51.95682	55.4491	26.94557	49.00349	100	85.59143
	130	3.12	4.541333	50	52.76074	35.71429	48.13084	100	69.56522

Table 6

Summary of renal function measured by blood and urine chemistry for the group of acceptable perfusion.

Min.	GFR Glomerular Filtration Rate ml/min	FF Filtration Fraction (%)	VFR Volume fraction reabsorb (%)	Tubular Reabsorption [Na] (%)	[K] (%)	[Cl] (%)	[Prot] (%)	[Glu] (%)
bit 3								
15	3.223579	6.316356	71.21212	69.30564	0.142045	68.12771	100	98.49475
45	4.632833	7.071167	68.42105	68.42105	56.72515	66.10333	100	95.20993
75	3.697231	4.967155	59.375	63.94531	54.73214	62.22588	100	89.04718
98	2.6915	3.598127	42.85714	45.97403	30	44.32234	100	71.96262
105	2.708875	3.679981	38.46154	42.14648	23.45216	39.51348	100	66.32801

WHAT IS CLAIMED IS:

1. A method for perfusing an organ with a fluid, comprising:

connecting an organ to a fluid system, the fluid system including at least a controller and a monitor;

flowing fluid from the system into the organ and perfusing the fluid through the organ;

monitoring organ characteristics and fluid characteristics;

communicating monitored organ characteristics data and fluid characteristics data to said controller; and

controlling with said controller at least one member selected from the group consisting of flow, contents and physical characteristics of the fluid as a function of said monitored data.

2. A method according to claim 1, wherein said controller compares said monitored organ characteristics data and said monitored fluid characteristics data to reference organ characteristics data and reference fluid characteristics data, and controls said system to minimize differences between said monitored data and said reference data.

3. A method according to claim 2, wherein said monitored fluid characteristics data includes fluid pressure data and said reference fluid characteristics data includes reference fluid pressure data reflecting a pressure of the fluid needed to perfuse the fluid through the organ, and the controller controls a pump to regulate the pressure of the fluid in the fluid system and in the organ.

4. A method according to claim 1, wherein said system comprises a piston-cylinder blood pump controlled by said controller.

5. A method according to claim 1, further comprising determining viability of said organ with said controller as a function of said monitored data.

a controller in data communication with said monitors and controlling at least one member selected from the group consisting of flow, contents and physical characteristics of the fluid flowed through said connector as a function of data received from said monitors.

14. An apparatus according to claim 13, further comprising a position-adjustable organ holder.

15. An apparatus according to claim 13, further comprising a temperature, humidity and sterility controlled enclosure for an organ connected to the connector.

16. An apparatus according to claim 13, wherein the organ characteristics monitor comprises a weight sensor, and the controller comprises a weight comparator and a fluid flow adjustment actuator to adjust flow of fluid through the connector to an organ responsive to a weight change of an organ.

17. An apparatus according to claim 13, wherein said connector comprises an adjustable piston cylinder blood pump a stroke of the adjustable piston cylinder blood pump controlled by the controller to adjust pressure of a fluid flowing through said connector into an organ.

18. An apparatus according to claim 13, wherein said fluid characteristics monitor comprises at least one member selected from the group consisting of an oxygen partial pressure sensor, a carbon dioxide partial pressure sensor and a pH sensor, and the controller comprises at least one comparator and at least one adjustment actuator to adjust a corresponding at least one member selected from the group consisting of oxygen partial pressure, carbon dioxide partial pressure and pH of fluid flowing through the connector to an organ responsive to data received from said fluid characteristics monitor.

19. An apparatus according to claim 16, wherein the organ characteristics monitor comprises a temperature sensor, and the controller comprises a temperature comparator and a flow adjustment actuator to adjust

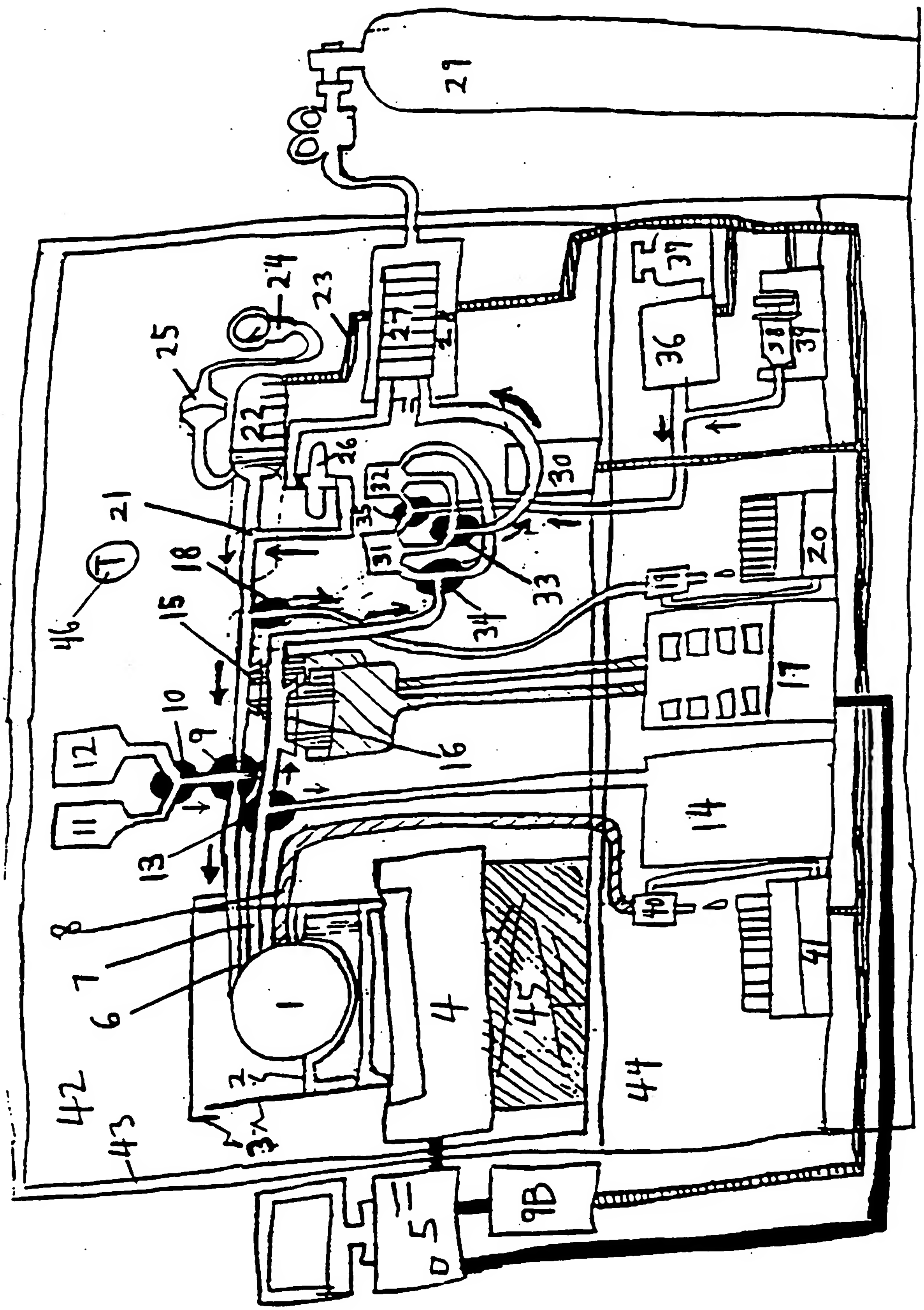


FIG. 1

Fig. 3

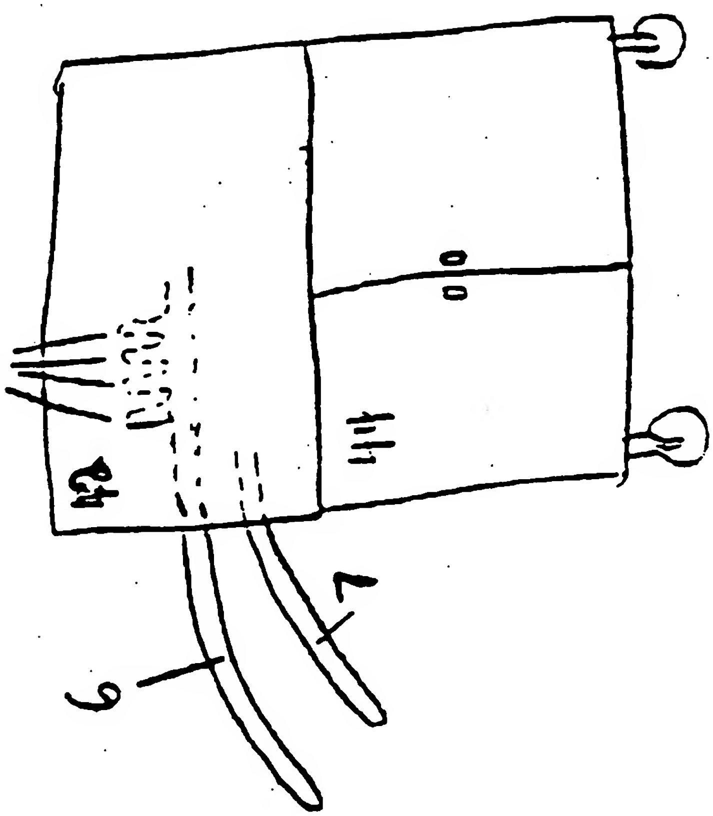
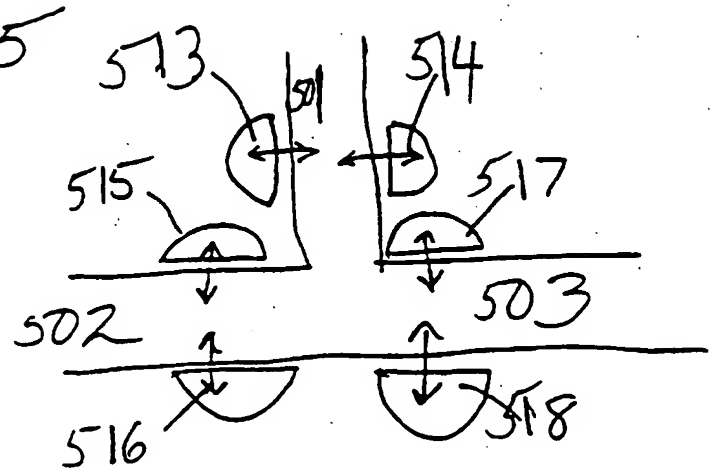
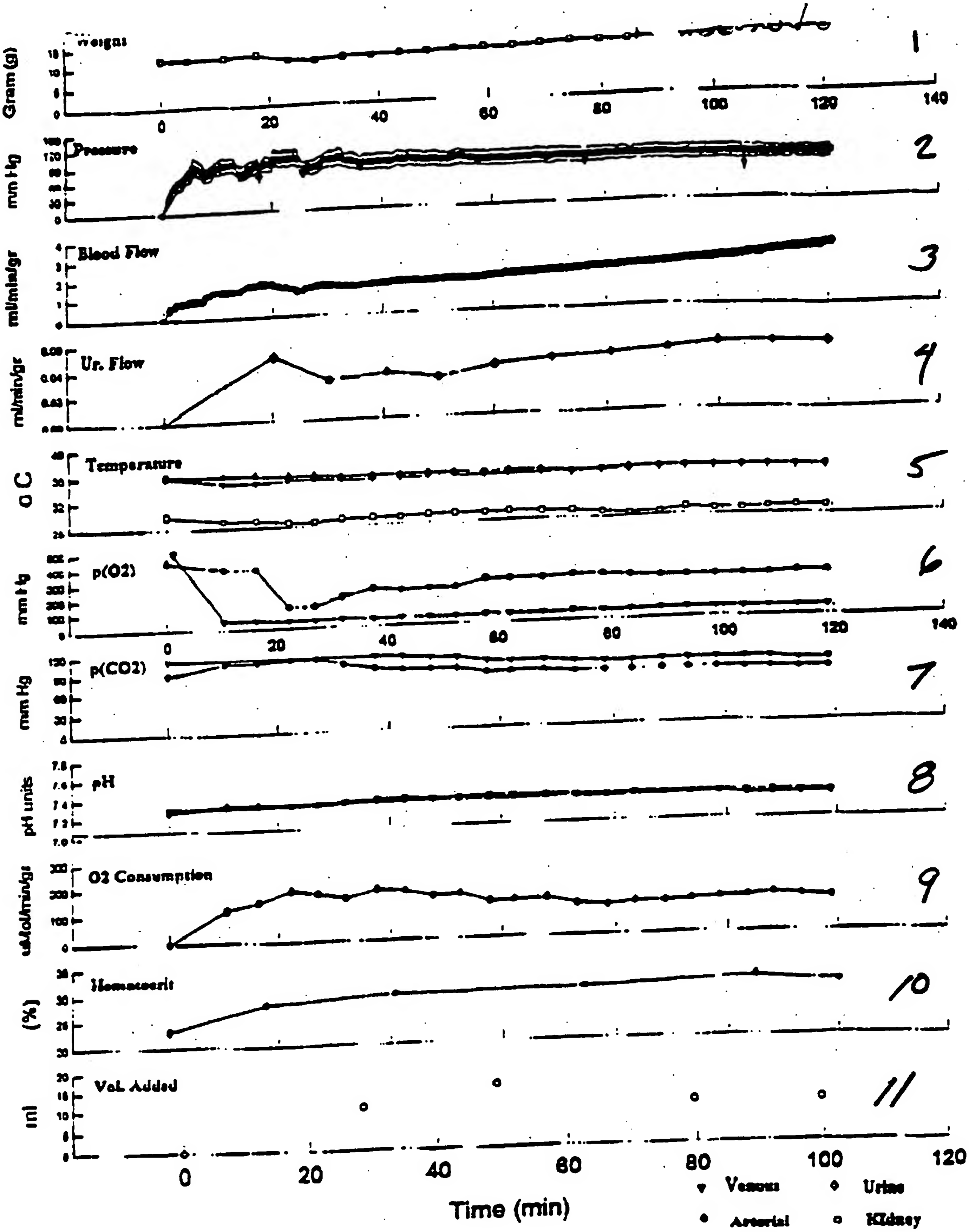


FIG 5





Weight
Gram (g)
Pressure
mm Hg
Blood Flow
ml/min/gr
Ur. Flow
ml/min/gr
Temperature
C
p(O2)
mm Hg
p(CO2)
mm Hg
pH
pH units
O2 Consumption
Hematocrit
(%)
Vol. Added
ml
1
2
3
4
5
6
7
8
9
10
11
0
20
40
60
80
100
120
140
Time (min)
Venous
Urine
Arterial
Kidney

FIG 6

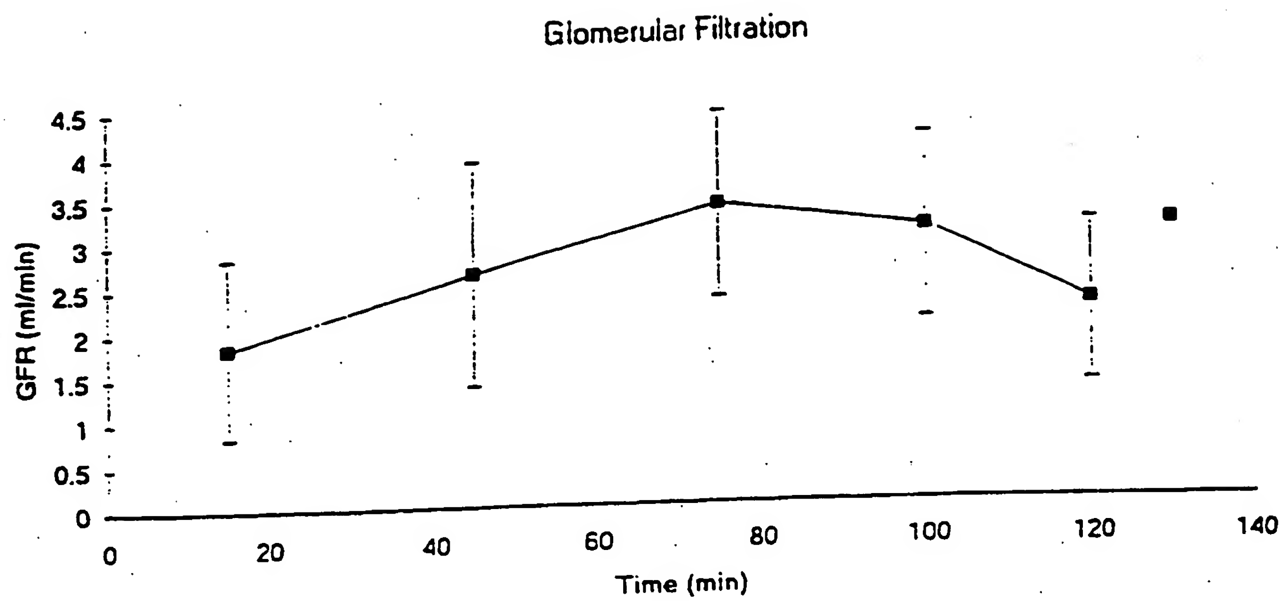

Glomerular Filtration
GFR (ml/min)
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
0
20
40
60
80
100
120
140
Time (min)

FIG 9

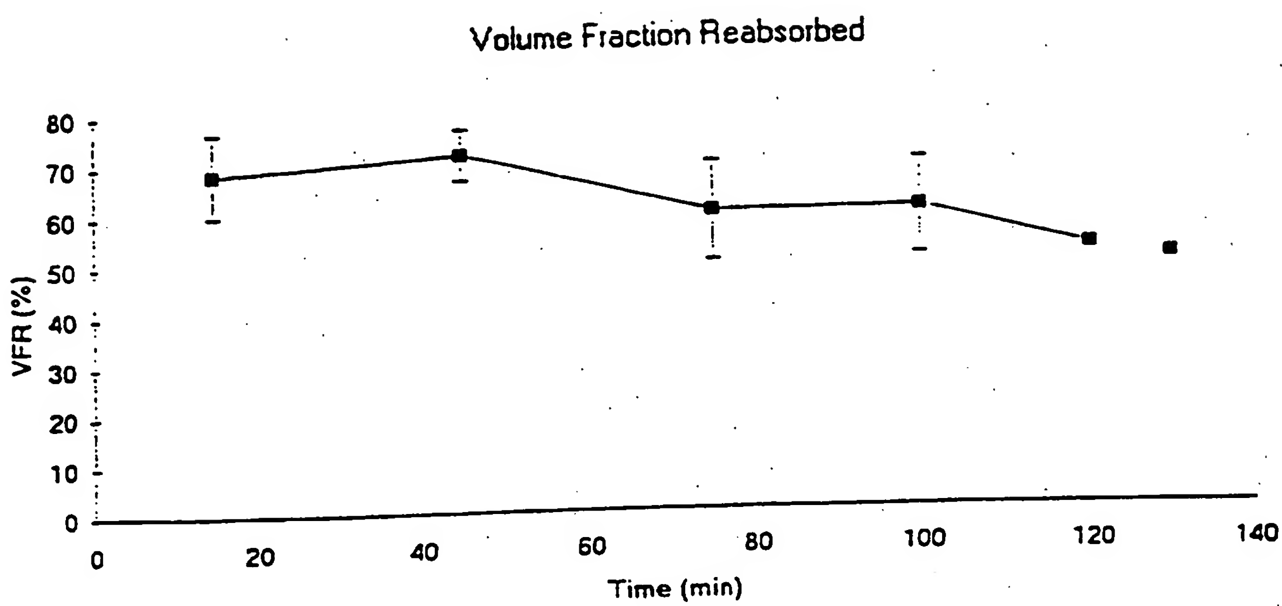

Volume Fraction Reabsorbed
80
70
60
50
40
30
20
10
0
VFR (%)
0
20
40
60
80
100
120
140
Time (min)

FIG 11

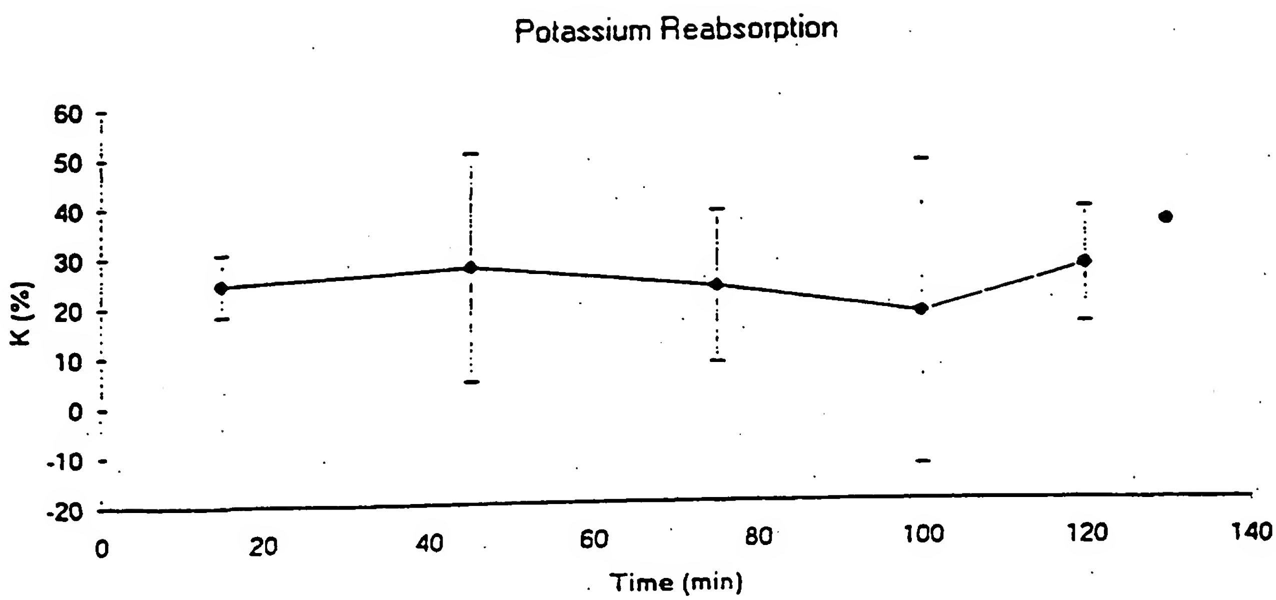

Potassium Reabsorption
60
50
40
30
20
10
0
-10
-20
K (%)
0
20
40
60
80
100
120
140
Time (min)

FIG 13

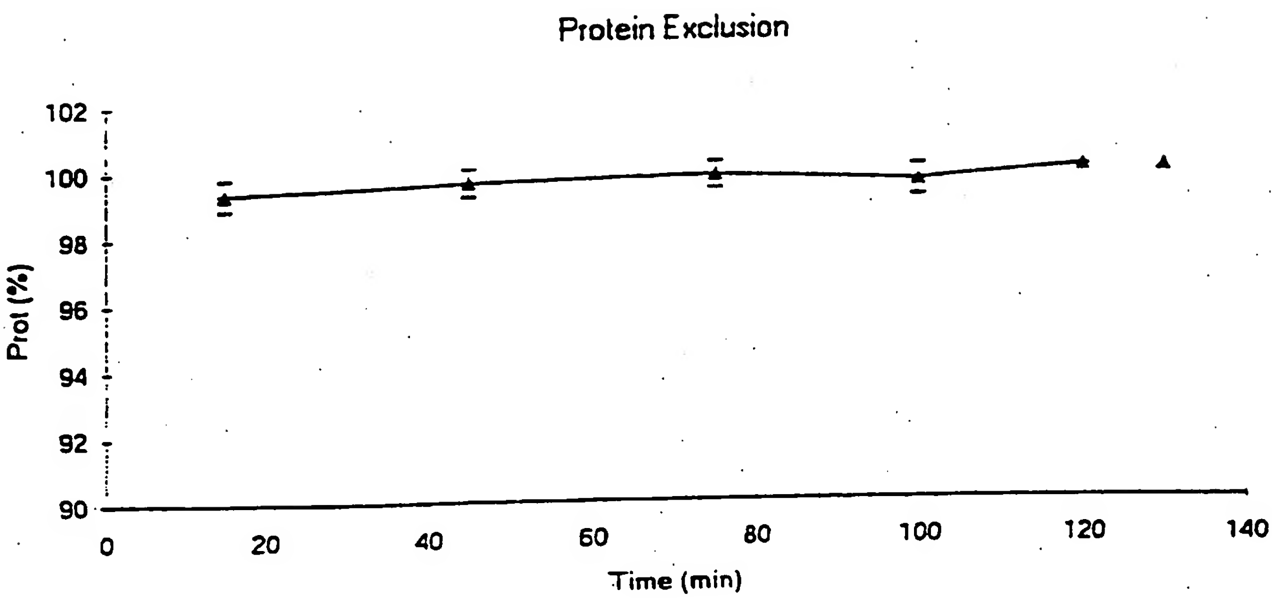

Protein Exclusion
102
100
98
96
94
92
90
Prot (%)
0
20
40
60
80
100
120
140
Time (min)

FIG 15

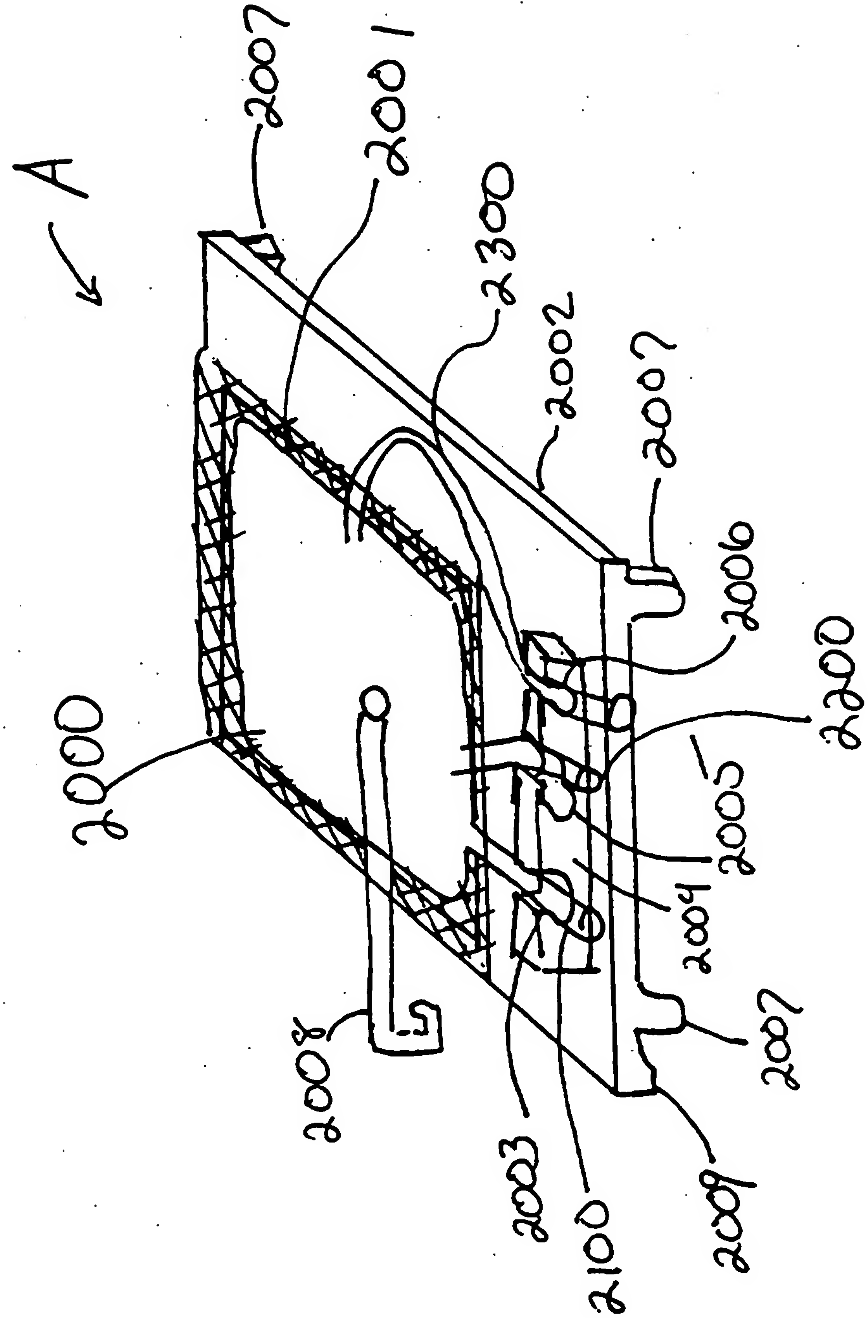

A
2007
2001
2300
2002
2007
2006
2200
2005
2004
2000
2008
2003
2100
2009
2007

FIG 17

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/04205

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Database WPIDS on STN, Derwent Publications Ltd., WPIDS No. 90-358177, JP 02-258701 A (OLYMPUS OPTICAL CO LTD) 19 October 1990 (19.10.90), abstract.	16, 19
A	US 4,666,425 A (FLEMING) 19 May 1987 (19.05.87), see entire document.	1-22
A	US 5,141,847 A (SUGIMACHI ET AL.) 25 August 1992 (25.08.92), see entire document.	1-22
A	US 5,338,662 A (SADRI) 16 August 1994 (16.08.94), see entire document.	1-22
A, P	US 5,472,876 A (FAHY) 05 December 1995 (05.12.95), see entire document.	1-22
A	SCHOLZ et al. Organ Preservation Machine OKM 82. medizintechnik. 1983, Vol.23, No. 1, pages 2-5.	1-22
A	PACINI et al. Excellent Performance of the Isolated Rabbit Kidney Perfused with Platelet and Leukocyte-Poor Blood. Boll. Soc. Ital. Biol. Spec. 1980, Vol. 56, pages 2497-2503.	1-22
A	RIJKMANS et al. Six-Day Canine Kidney Preservation. Transplantation. 1984, Vol. 37, No. 2, pages 130-134.	1-22
A	PACINI et al. An Analysis of the Optimal Conditions for Perfusing an Isolated Rabbit Kidney with Homologous Blood. Renal Physiol. 1983, Vol. 6, pages 72-79.	1-22
A	US 5,285,657 A (BACCHI ET AL.) 15 February 1994 (15.02.94), see entire document.	1-22